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37. The method of claim 34 wherein the second component is von Willebrand factor conjugated with a ligand.

38. The method of claim 37 wherein the second component is conjugated to biotin.

39. The method of claim 12 wherein the binding agent binds to a ligand/receptor complex comprising VEGF/VEGF receptor.

REMARKS

This response is in response to the office action mailed 29 January 2002. Entry of the above is respectfully requested.

Following the entry of this amendment claims 12, 14, 17- 18, and 29-39 are pending. In view of the amendments set out above and the following remarks, reconsideration is respectfully requested. Applicants attach a red-line copy of the claims that reflect the amendments made in this amendment.

Paragraph 3 suggestion

Following the suggestion in the Office Action, Applicants have replaced the previous sentence (concerning the provisional application, and submitted in the Supplemental Response filed 20 November 2001) with a sentence that includes both the provisional application and the PCT application.

Paragraph 6 rejection

Claims 12-14, 17-21, and 29-32 have been rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. All of the focus of this rejection appears to be related to Applicants' use of the phrase "bifunctional binding agent" in Claim 12. Since Applicants have amended the claim to remove this phrase, it is respectfully suggested that this rejection is now moot.

However, deleting of the phrase "bifunctional binding agent" from the claims should not be taken as acquiescence with or agreement to the arguments presented in

the office action concerning this phrase. Applicants have amended the claims to reflect the methodology used in their in vitro and in vivo examples, for the sole purpose of advancing prosecution as quickly as possible. It is intended that the bifunctional binding agent concept, as defined in the specification and examples, will be prosecuted in a continuing application, reflecting Applicants strong opinion that this phrase is properly and adequately enabled.

Regarding basis for the amendments to claims 12 and 18, basis for the amendments can be found throughout the specification and in Examples 6-8, among other places. The "binding agent" is disclosed throughout the specification. See for example, page 11, lines 6-12, page 1, lines 16-19, and page 13, lines 1-9, among other places. The "first component for binding the binding agent to a pre-selected site" concept is disclosed in Examples 6-8, page 1, lines 16-19, page 11, lines 6-12, page 12, lines 6-15, and page 13, lines 21 et seq., among other places. The "administering a second component" language and its use to bind platelets is disclosed in Examples 6-8, page 1, lines 16-19, page 11, lines 6-12, and page 12, lines 6-15, among other places.

Claim 14 has been amended so that the claim is limited to the subject matter elected pursuant to the election requirement mailed 16 January 2001, and to conform the language to that used in independent claim 12.

Claim 17 has been amended so that the claim is limited to the subject matter elected pursuant to the election requirement mailed 16 January 2001, and to conform the language to that used in independent claim 12. Addressing the comments in the Office Action directed to enablement of claim 17, the claim has now been limited to an element about which it is well known that it specifically binds platelets. There is a significant amount of prior art proving this point, but for the sake of simplicity, Applicants merely direct attention to the Appendices submitted as a part of the response filed 23 July 2001.

Regarding claim 19, since this claim has now been cancelled, this portion of the rejection is now moot.

Regarding claims 29-32, it is respectfully submitted that these claims are enabled for the same reasons that claim 12 is enabled, as detailed above. Further, the use of these specific sites is well known to those of ordinary skill in the art. See for

example, the two Thorpe references cited in the previous office action.

Since the targeting component and the platelet-binding component in Claim 12 are not new elements of the claimed invention, the language now used conforms the claim to the working examples, and the Office Action does not have art cited against the claims, it is respectfully suggested that the claims are now in condition for allowance.

Reconsideration is respectfully requested.

THE PARAGRAPH 8 REJECTION

Claims 29-32 have been rejected under 35 U.S.C. 112 for lacking antecedent basis for "pre-selected site." Claim 12 has been amended, as noted above, to include this language. Reconsideration is respectfully requested.

REGARDING THE NEW CLAIMS

Claims 33-38 have been submitted in response to the Office Action's suggestion that claims directed to the working examples would implicitly not be subject to an enablement rejection. These various elements have now been included in these dependent claims.

Basis for "biotin ligand" in claim 33 can be found at page 13, lines 11+, among other places.

Basis for the anti-ligand in claims 34 and 35 can be found at page 13, lines 15-16, among other places.

Basis for von Willebrand factor conjugated to a ligand in claims 36-38 can be found at page 13, lines 8+ and 15+, among other places.

Regarding claim 39, basis for this claim can be found in original claims 19-21, and has been submitted to address the enablement issue raised in the office action regarding claim 19. The claim now recites a well known ligand/receptor complex.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at 301-203-6300 (a local call).

Respectfully submitted,

March 11, 2002



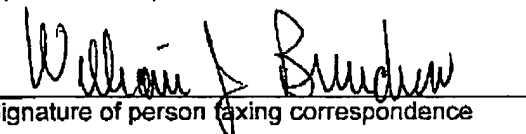
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Certificate of Mailing by facsimile (37 CFR 1.8): I hereby certify that this supplemental response and clean copy of claims is being transmitted to Examiner DeCloux (fax number 703-746-4982) on 11 March 2002.

William J. Bundren
typed name of person mailing correspondence



Signature of person faxing correspondence

Red-line copy of all claims:

12 (thrice amended). A method of inducing a thrombus in vivo comprising:
administering [a bifunctional binding agent comprising a targeting] a binding agent having a first component for binding the binding agent to a pre-selected site [and a component that specifically binds platelets];
administering a second component, said second component specifically binds platelets, and allowing the second component to bind to the binding agent;
binding platelets on the [binding agent] second component;
inducing activation of the platelets; and thereby
allowing a thrombus to form.

13. CANCELLED

14 (amended). The method of claim 12 [13] wherein the [targeting] binding agent is one or more binding agents selected from the group consisting of an antibody, and fragments or parts thereof [a monoclonal antibody, a polyclonal antibody, a humanized monoclonal antibody, a chimeric antibody, a single chain antibody, a dimeric single chain antibody construct, a multimeric single chain antibody construct, a peptide, a nucleic acid sequence, a protein, a ligand, an oligonucleotide, conjugates that include any one of the above, fragments or parts of any of the above, and functional equivalents of the above].

15. CANCELLED

16. CANCELLED

17 (thrice amended). The method of claim 12 wherein the second component [that specifically binds platelets] comprises [at least one of the components selected from the group consisting of] von Willebrand factor[, osteopontin, fibrinogen, fibrin, fibronectin, vitronectin, collagen, thrombospondin, laminin, heparin, heparan sulfate, chondroitin sulfate, phospholipase A2, matrix metalloproteinases, thrombin, glass, sialyl-lewis X, fibulin-1, PECAM, ICAM-1, ICAM-2, p-selectin ligand, MAC-1, LFA-1, and portions of any of the above].

18 (thrice amended). The method of claim 12 wherein the first component, the second component, or both, [bifunctional binding agent] further comprise[s] a moiety selected from one or more of the following: biotin, homophyllic peptides and human Fc fragments.

19. CANCELLED

20. CANCELLED

21. CANCELLED

22. CANCELLED

23. CANCELLED

24. CANCELLED

25. CANCELLED

26. CANCELLED
27. CANCELLED
28. CANCELLED

29. The method of claim 12 wherein the pre-selected site comprises subendothelium.

30. The method of claim 12 wherein the pre-selected site comprises tumor-associated antigen.

31. The method of claim 12 wherein the pre-selected site comprises tumor-specific antigen.

32. The method of claim 12 wherein the pre-selected site comprises hyperplastic tissue.

New Claims:

33. The method of claim 14 wherein the binding agent further comprises a biotin ligand. [from page 13, line11+]

34. The method of claim 12 wherein allowing the second component to bind to the binding agent comprises administering an anti-ligand that specifically binds the binding agent.

35. The method of claim 34 wherein the anti-ligand is an anti-ligand selected from the group consisting of avidin, streptavidin, neutravidin, and derivatives and analogs thereof. [from page 13, lines 15-16]

36. The method of claim 17 wherein the second component is von Willebrand factor conjugated with a ligand [from page 13, lines 8-9, 15+]

37. The method of claim 34 wherein the second component is von Willebrand factor conjugated with a ligand.

38. The method of claim 37 wherein the second component is conjugated to biotin.

39. The method of claim 12 wherein the binding agent binds to a ligand/receptor complex comprising VEGF/VEGF receptor.